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Review

The South African guidelines on Enuresis—2017

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Treatment guideline;
Expert consensus

Abstract
Introduction: Enuresis (or Nocturnal Enuresis) is defined as discreet episodes of urinary incontinence during sleep in children over 5 years of age in the absence of congenital or acquired neurological disorders.
Recommendations: Suggestions and recommendations are made on the various therapeutic options available within a South African context. These therapeutic options include; behavioural modification, pharmaceutical therapy [Desmospressin (DDAVP), Anticholinergic (ACh) Agents, Mirabegron (β3-adrenoreceptor agonists), and Tricyclic Antidepressants (TCA)], alternative treatments, complementary therapies, urotherapy, alarm therapy, psychological therapy and biofeedback. The role of the Bladder Diary, additional investigations and Mobile Phone Applications (Apps) in enuresis is also explored. Standardised definitions are also outlined within this document.
Conclusion: An independent, unbiased, national evaluation and treatment guideline based on the pathophysiological subcategory is proposed using an updated, evidence based approach. This Guideline has received endorsement from the South African Urological Association, Enuresis Academy of South Africa and further input from international experts within the field.

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Introduction

These guidelines are based on national meetings (Phase 1) held at the Department of Paediatric Urology, Rahima Moosa Mother & Child (Coronation) Hospital, Johannesburg in November 2015, and (Phase 2), held at the Boston Scientific Centre of Excellence, Bryanston, Johannesburg in February 2016. These meetings were held to achieve local national consensus. To avoid any bias, this guideline received added input and suggestions from 3 independent international experts in the field of Paediatric Urology. Furthermore, pharmaceutical trade names are not written within this document. Pharmaceutical companies and their representatives did not have any access to this document during any of the stages of its write-up, format or publication. Contributing authors have not received any honoraria for their involvement in this guideline. An attempt is made to define, outline, caution, highlight and suggest an acceptable treatment algorithm guideline for use in the management of children suffering from Enuresis, within a South African setting. These guidelines are aimed at general practitioners, paediatricians, urologists, paediatric nephrologists and hospital administrators, within the private and public sectors of South Africa. We further aim to update this guideline 3 yearly due to the rapid advancements within this field of Medicine. Local barriers with implementing this guideline include drug availability, costs, resources and medical staff shortages. Recommended dosages are to be tailored to patient habitus, weight, and renal function where necessary and must be cross referenced with an updated acceptable Medical Reference source where needed. This guideline has been structured as a more comprehensive update to the previous local Guideline [1].

This guideline has been endorsed by the:

South African Urology Association (SAUA), Enuresis Academy of South Africa and members from the South African Paediatric Nephrology Society.

Definitions and terminology [2]

Definition*:

Enuresis (or Nocturnal Enuresis) is defined as discreet episodes of urinary incontinence during sleep in children over 5 years of age in the absence of congenital or acquired neurologic disorders.

Enuresis can be divided into Mono-Symptomatic Enuresis (MSE) or Non-Mono-Symptomatic Enuresis (NMSE).

Monosymptomatic Enuresis (MSE):

Isolated Enuresis without other Lower Urinary Tract symptoms (nocturia excluded), and without bladder dysfunction, is defined as Monosymptomatic Enuresis.

Primary Enuresis (PMSE)

Children who have not had a dry period of at least 6 months.

Secondary Enuresis (SMSE)

Children who have had a previous dry period of >6 months.

Non-Monosymptomatic Enuresis (NMSE)

Children with enuresis and any other Lower Urinary Tract symptoms, such as daytime wetting or urgency are said to have Non-Monosymptomatic Enuresis.

The severity of enuresis can be defined as

frequent (>4 per week) or **infrequent** (<4 per week).

Expected Bladder Capacity (EBC) can be defined by the following published formulas [3–5]:

Koff's formula for EBC [3]:

EBC (ml) = 30 × (age in years + 2)

Hjälmås's formula, **more widely used formula** for EBC [4]:

EBC (ml) = 30 + (age in years × 30)

Kaefer's formula for EBC [5]:

if age less than 2 years old:

EBC = 2 × age (years) + 2 = capacity (ounces*)

if age 2 years old or older:

EBC = age (years) [divided by] 2 + 6 = capacity (ounces*)

*Conversion from ounces (oz): ml is roughly 1:30.

Girls have been observed to have larger EBC than boys, BUT this discrepancy was not significantly significant [5].

Nocturnal (night-time) Polyuria is defined as nocturnal urine output exceeding 130% of EBC for age [1].

Nocturia is the complaint that the child has to wake at night to void. Unlike enuresis, nocturia does not result in incontinence, and nocturia is not necessarily indicative of a pathologic condition.

***For the purpose of this guideline: Primary Mono-Symptomatic Enuresis (PMNE) will be discussed, unless otherwise specified**.

Prevalence & associated factors

The prevalence of enuresis episodes varies in children and decreases with age, with higher rates in the less developed countries [6,7]. In a recent South African study, the overall prevalence of NE was 16.0%, with 14.4% of children suffering from mono-symptomatic NE (MNE) and 1.6% from NE with daytime urinary incontinence [8].

The male:female prevalence ratio of NE was 2:1 [8].

Associations between NE, poor school performance and learning problems have been reported. In addition, NE may result in low self-esteem, leading to psychological problems [8].

Parental involvement and perceptions

Parents often treat enuresis as a psychological problem. Therefore, parental perception can often cause psychological damage to children suffering from NE, through punishment, shaming and lack of support. Parental concern is often not high and as a result, most children are not treated at all. The latter is partly because the condition often resolves spontaneously, or parents are unaware of treatment modalities. Families tend to self-treat their children with behavioural strategies such as fluid restriction, waking the child at night to void and counselling. These treatment strategies have a low success rate [8].

Pathophysiology

The 'three systems model'

In 2000 Butler and Holland, proposed a "three systems model" for understanding PMSE [9]. The value of this model is that it helps conceptualise therapeutic interventions. Enuresis is caused by one or more of the following three "systems" (see Fig. 1):

1) nocturnal polyuria associated with abnormal diurnal variations of antidiuretic hormone (ADH)/arginine-vasopressin release during sleep,
2) detrusor overactivity/over active bladder [OAB],
3) abnormal sleep/arousal patterns.

The "three systems model" can also assist to outline a management strategy for children who do not respond to standard treatment. Vander Walle et al. have suggested that a combination assessment of the

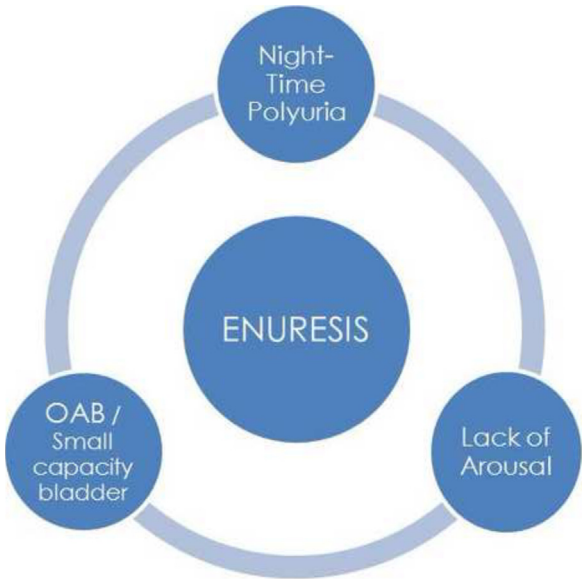

Fig. 1 The "three systems" model—adapted from Butler et al. [9].

above factor will identify subtypes of PMSE [below] and guide treatment [11].

1. Normal urine output at night and normal bladder capacity might respond to either DDAVP or the alarm.
2. Small bladder capacities for age are likely DDAVP-resistant and might respond to the alarm.
3. Children with nocturnal polyuria and normal bladder capacity should respond to DDAVP.
4. Children with nocturnal polyuria and reduced bladder capacity may find combined therapy of alarm and DDAVP to be successful [10,11].

For the purpose of simplicity within this guideline, we have summarised the 4 above subtypes into 3 [see algorithm Fig. 2—algorithm].

The "bladder–brain dialogue" [12]

Another entity that has been observed in severe (refractory)* enuresis is a phenomenon of long-term overstimulation from bladder signals, which suppress the functioning of the arousal center, thus affecting the brain arousability in affected children. Thus, overstimulation of this "bladder–brain dialogue" is postulated to result in a lighter sleep, but difficulty with complete awakening, in children with severe (refractory)* enuresis.

*According to their study, severe (refractory) enuresis was defined as ≥5 wet nights per week [12].

Behavioural modification

Behavioural modification includes:

General behavioural modification.

Water intake.

Toilet behaviour.

General behavioral modification [13]

Behavioural interventions/modifications propose that the nightly 'dry state' is a learned response which can be accomplished using psychological conditioning methods.

Published methods include:

Fluid restriction

Fluid restriction limits nocturnal urine production, thus reducing nocturnal voiding demands. Day time restriction may worsen enuresis episodes buy reducing the 'Bladder Volume: Nocturnal Urine Production' ratio.

'Lifting'

Parents/caregivers 'lift up' the child while still asleep, and take them to the bathroom where urination is encouraged.

Scheduled wakening

Involves scheduled wakening, with the sleep being interrupted and the child asked to void during the night.

Star charts and other reward systems

This method uses a positive reinforcement method to promote a change in behaviour.

Bladder training and retention control training

Attempts at increasing the bladder capacity is proposed by:

Increasing day-time fluid intake,

Delaying micturition [where possible],

Stream interruption exercises.

Conclusion and comparative assessment review of the overall effect of the above

The above interventions were proven effective compared to no treatment, BUT did not outperform active treatment methods [13].

Water intake in children

Recommend as is appropriate, also see Scientific Opinion on Dietary Reference Values for water:

http://www.efsa.europa.eu/en/efsajournal/pub/1459.

Toilet behaviour

Encourage the child to always use the toilet before going to bed

Easy access, adequate lighting, to the bathroom must be in place

Toilet position

If seat too big the child 'falls in', thus can be obstructing urethral outlet,

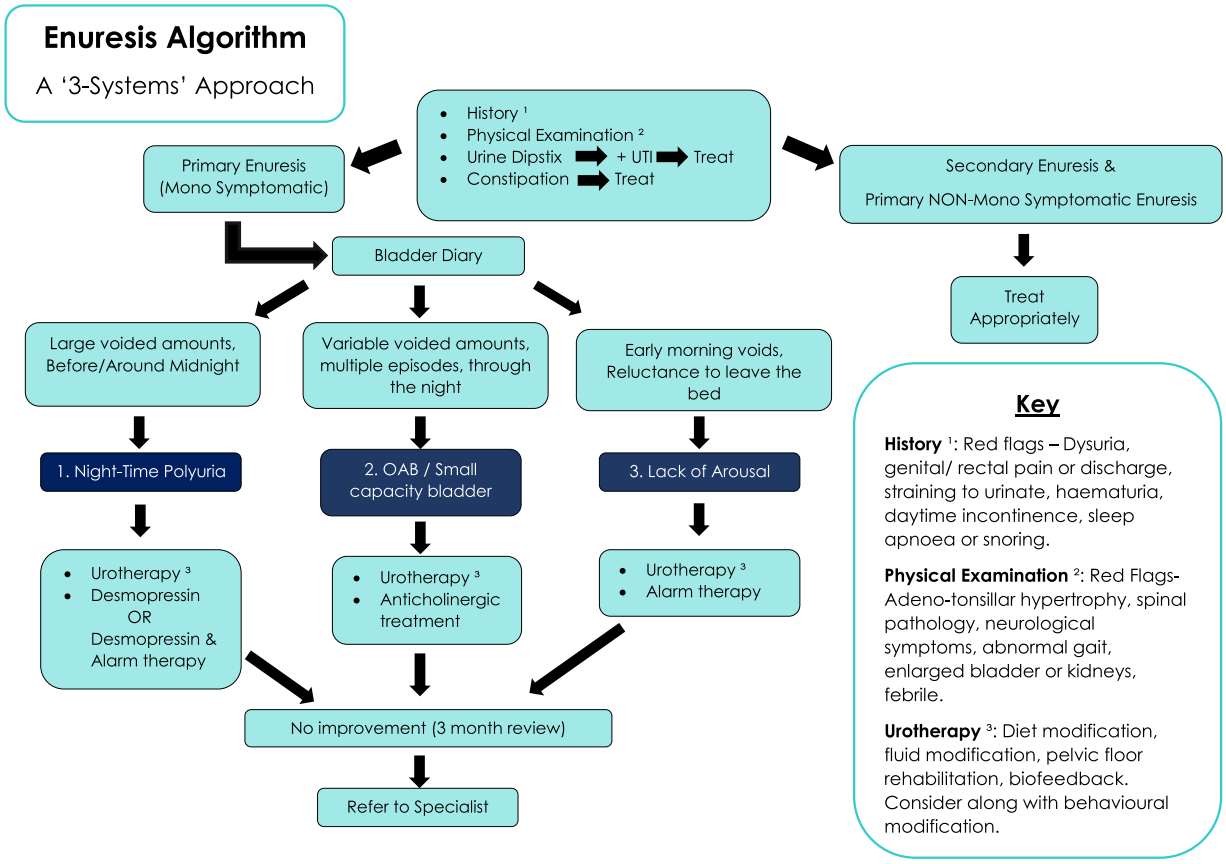

Fig. 2 An algorithm for the approach to enuresis [Management Algorithm—portrait view].

Lean forward with elbows resting on thighs,

Feet should be resting on a foot stool/platform/ground,

Encourage overall hygiene.

Pharmaceutical therapy

Desmospressin (DDAVP)

DDAVP is the synthetic equivalent of the posterior pituitary hormone, vasopressin (AntiDiuretic Hormone (ADH)).

Monotreatment in cases of **Nocturnal Polyuria** has been recommended.

DDAVP is preferred for camps and sleepovers. A trial to test the response is suggested 6 week prior.

Although hyponatreamia is uncommon, fluid intake **should be avoided** an hour before and 8 h after taking the medication.

Duration of action may be prolonged if administered in a fasting state [14].

Contraindications: Hyponatraemia, renal failure, known hypersensitivity [15].

Formulations available

Oral tablet:

Initial dose: 0.2 mg (Max 0.4 mg) daily.

Only consider dose escalation after 2 weeks of initial treatment. Caution with escalation; prolonged bioactivity is suspected if children do not have a morning void. If this is the case, the dose should not be increased.

DDAVP nasal spray

Caution: Over-dosage reports resulting in seizures and hyponatraemia with Nasal Spray administration have limited the use of this route in the management of enuresis—FDA ALERT [12/4/2007].

MELT [oral desmopressin lyophilisate]

Suggested/recommended MELT dosage (120 mcg, 240 mcg) daily.

Children showed a preference to MELT formulation in a randomised study of MELT vs tablet formulation [16].

Although structured withdrawal programs did not show benefit previously [17], newer meta-analysis reported on better overall outcomes with a dose-dependent structured withdrawal regimen [18].

MELT [Oral Desmopressin lyophilisate] formulation has recently been made available in South Africa.

In conclusion, DDAVP can be used as monotreatment or in combination with alarm therapy [19].

Anticholinergic (ACh) agents

Efficacy, sub types, recommended dosages

High-quality evidence for/against anticholinergic medication as sole/combination therapy in PMNE is lacking [20]. Small functional bladder capacity associated with Nocturnal Enuresis is an indication to consider anticholinergics.

Types of anti-cholinergics:

Oxybutynin is widely used, but fesoterodine, tolteridine, solifenacin are also effectively used in treating the bladder overactivity component in children [21]. Oxybutynin has more side effects, but the newer anticholinergic agents are not yet registered for the use in children in South Africa, but are being used effectively nonetheless [22,23].

Recommended/suggested dosage:

Oxybutynin: children over 5 years; 5 mg up to 3 times daily.

Potential off label use:

Tolterodine: 0.12 mg/kg daily dose [24].

Solifenacin: 0.1–0.2 mg/kg daily dose. Solifenacin is currently used off label in South Africa, but is available as a 5 mg, 10 mg tablet [25].

The Anticholinergic 'Patches' are not yet available in South Africa, at the time of writing.

Contraindications: Myasthenia Gravis, glaucoma, hypertension, Downs syndrome, known hypersensitivity.

Complications, compliance

In adults, anti-cholinergics are well documented regarding efficacy and tolerability. In children, however, evidence-based studies are limited and vary across these compounds. This is demonstrated by different levels of evidence and grades of recommendation for oxybutynin (Grade 3C), propiverine (Grade 1B/C), tolterodine (Grade 3C), and trospium chloride (Grade 3C) awarded by the International Consultation on Incontinence [26].

Studies show that adverse effects were less frequent in children than in adults [21]. Common side effects include dry mouth and eyes, constipation, facial flushing, drowsiness and cognitive effects [27].

*Mirabegron (**β**3-adrenoreceptor agonist)*

Mirabegron, is a β3-adrenoreceptor agonist used in the management of Over Active Bladder [OAB] [28].

A recent 'pilot' study has been performed in children with *isolated* OAB intolerant/refractory to ACh therapy. Daytime continence improved in 52 of 58 patients recruited. Only 8 patients reported on mild to moderate side effects from therapy [28].

The precise role of Mirabegron (β3-adrenoreceptor agonist) in the management of Enuresis with an OAB component, may seem promising. But since this therapeutic option has not yet been explored, this agent cannot be recommended as routine therapy within this current guideline.

Imipramine—Tricyclic Anti-Depressant [TCA]

Imipramine is a Tricyclic Antidepressant associated with a 50% response rate and is thought to act through brainstem central sympathomimetic/noradrenergic action promoting arousal and inhibiting micturition [29]. Imipramine also increases the nocturnal antidiuretic hormone (ADH) excretion restoring the morning plasma levels of ADH [30]. It is recommended that imipramine only be used in therapy resistant older children with attention deficit hyperactivity who are severely distressed by their condition, when primary and second line treatments (the alarm, desmopressin, basic urotherapy and anti-cholinergics) have failed. In the case of a child with a family history of unexplained cardiac death, or who complains of syncope and heart palpitations, prolonged QT syndrome must be excluded with electrocardiogram recording [31]. Psychological side effects like mood changes may be bothersome during the first weeks of therapy but usually recedes without dosage change. Drug holidays are important to prevent tolerance and one strategy is to stop therapy after every 3 months for at least 2 weeks. Imipramine therapy may be combined with the bed alarm or desmopressin. However, Imipramine combined with alarm therapy did not show superior effectiveness compared with alarm therapy in isolation [32,33].

Dosage utilised: 25 mg–50 mg daily one hour before bedtime [34].

Caution: TCAs are highly metabolised by Cytochrome (Cyt) P450 so concurrent use of drugs that inhibit Cyt P450, may cause TCA toxicity. Also beware of other concurrent medication usage which may also cause QT prolongation.

Recommendations when TCA is used as therapy for enuresis:

a. The child has no response to all other treatments.
b. When a team with expertise in bedwetting evaluated the child and determined that the alarm and/or desmopressin therapy has failed.
c. Parents must be informed on how imipramine works and that not all children will experience improvement.
d. The parents must know that the dose must be increased gradually and when the therapy is discontinued also withdrawn gradually.
e. Cardio-toxicity is a potentially lethal condition associated with over dosage in children.
f. The initial course is three months, and there is a high relapse rate when therapy is stopped. Restarting to be decided on a case by case basis.
g. Imipramine must be stored and locked in a safe place out of the reach of other children.
h. Baseline pre-treatment evaluation must include: History (including family history), BP, Pulse and Resting ECG [34].
i. Various published opinions, expressing the **pros and cons** of Imipramine usage from South African and international expert

editorial correspondence needs to be considered when reviewing cost issues while counselling parents/care givers [35,36].

j. Evidence does support a positive response during active treatment phase with TCAs, but relapse rates are significant on cessation. Combination therapy with anti-cholinergics have been observed to outperform tricyclic usage in isolation [20].
k. Combination (Imipramine & Oxybutynin) treatment was shown to be more effective than imipramine used in isolation (RR 0.68, 95% CI 0.50–0.94) [37].
l. Imipramine has a low therapeutic to toxin drug ratio. Fatalities have occurred in children at doses as low as 15 mg/kg [38].

Alternative treatment/complementary therapies

This includes the use of medicinal herbs, hypnosis, acupuncture, chiropractic therapy and psychotherapy. Some weak evidence to support the use in enuresis does exist, but the methodological approach used in most of these studies are non-scientific. To document the role of these agents in enuresis, future randomized trials are needed [39,40].

Urotherapy

Urotherapy refers to the conservative and behavioural adjustments that patients and parents can make and encompasses management from a wide field of healthcare professionals [2].

The aim is to improve the bladder control in 3 domains:

1. Increase bladder capacity,
2. Decrease night time urine output,
3. Sensitize unconscious awareness of bladder filling.

Techniques include; daily increase in fluid intake, reduced nightly intake, regular bladder emptying, pre-bedtime voiding, daily bowel action, functional awareness training, avoid caffeine and high sugar containing drinks [19,41].

Urotherapy encompasses the following standard components [2]:

(1) Information/demystification.
(2) Instruction.
(3) Life-style advice.
(4) Registration of symptoms and voiding habits (Diary/Apps).
(5) Support (encouragement) with the caregiver.

Significant improvement occurred in more than 70% of cases when Urotherapy was used as initial therapy [41].

Alarm therapy

Alarm therapy is based on a device that gives a strong sensory signal (mostly acoustic), immediately after an incontinence episode [2].

The 'Bed Wetting Alarm' is also known as the Bell and pad method or Bell and pad alarm therapy.

A sensor pad is placed within the underpants or on the bed sheet. This sensor is activated before reclining to sleep. Alarm triggering occurs during contact with 'wet' urine. The alarm is sounded, causing a sudden cessation in micturition. The child is then encouraged by the parent/care giver to wake up and complete the void.

The alarm should initially be worn every night, with treatment withdrawal evaluation at 12 weeks or if dry for 2 consecutive weeks.

Initiation of this therapeutic method requires a motivated family and environment who understand the potential disruptive nature of this treatment modality.

The child should be encouraged to manage the alarm and be part of the process. Combination and Isolation therapy can be considered.

Various types of alarms are available: Pad-type alarms/Wired alarms/Wireless alarms.

Excessive sweating may falsely trigger the alarm. Poor contact, faulty device or 'flat' batteries may cause device malfunction.

Online purchase from certain agencies within South Africa, costs approximately ZAR 300–ZAR 3000. Costs of the linen savers, batteries, laundry are also needed to be factored in, when counselling parents.

This modality should be combined with rewards and motivational encouragement.

Realistic published expected outcomes, observed initial response rates up to 84% and relapse rates of 30%. Furthermore, better outcomes are associated with patient willingness and female gender [42].

"Overlearning" (having a large drink before bed while continuing alarm training) in a child who has learnt to be dry by sleeping through the night may further reinforce waking to void if needed, and thus reduces relapse. If relapse occurs, repeating alarm training may also assist [43].

A recent Cochrane review further observed that alarm therapy was found to be superior to oxybutynin therapy (RR 3.25, 95% CI 1.77–5.98) [37].

Alarms using electric shocks were unacceptable to children or their parents and are no longer available.

Alarms may 'beeb', vibrate or play a recorded voice. However, there is insufficient evidence available to draw conclusions about the comparitive effectiveness of the different available alarm types [44].

Psychological issues

Psychological issues have been an accepted role player/co-existing factor in the pathogenesis of enuresis [45].

Psychological subclinical symptoms include:

guilt, sadness, humiliation, moodiness and embarrassment.

Clinical conditions associated with enuresis include:

Externalizing disorders [Conduct Disorder, ADHD].

Internalising disorders [Anxiety, Depression].

Mixed disorders [Anorexia, Autism Spectrum].

Psychological screening

Since clinicians may have limited consultation time during busy out-patient clinics, the following validated published psychological screening modalities can be performed in the waiting rooms:

- Short Screening Instrument for Psychological Problems in Enuresis (SSIPPE) [46].
- Child Behaviour Checklist (CBCL) [47].

Early referral

If an underlying psychological disorder is suspected, early referral for formal psychological assessment and management may be warranted as part of the multi-disciplinary approach to enuresis.

The high risk groups for a negative Impact on Quality of Life are: older age and female gender [48]. If confirmed by SSIPPE, these patients may merit fast tracked psychological treatment/referral.

Biofeedback

Biofeedback is a specific intervention of urotherapy that involves pelvic floor muscle retraining [2]. Biofeedback has been proven effective in the treatment of children with a functionally small bladder capacity. This method also allows children to hold larger (normal for age) volumes for longer periods, without any leaking episodes [49,50].

Mobile Phone Applications (Apps) in enuresis

The South African Smartphone market growth is amongst the highest in the world, with a yearly increase in growth of above 10% forecasted on each year, up to and including the year 2018 [51]. The electronic 'Bladder Diary' was observed to be less cumbersome and more user friendly and thus showed superiority over the traditional 'Pen and Paper' bladder diary [52].

These above factors make the use of Apps in the management of Enuresis a vital resource, especially since various Apps are custom designed for the management of this condition. Apps with Bladder Diary and management features are available on both the iOS (Apple) and Google Play Store (Android) platforms [53].

A recent independent review, ranked, evaluated and assessed all available Apps in the management of Enuresis. The top three performing Apps were ranked as: '*My Dryness Tracker*', '*Bedwetting Tracker*', and '*HapPee Time*' [53].

Referring doctors, therapists, patients and their families should be encouraged to embrace this technological adjunct in the evaluation, treatment and follow-up of enuresis.

Treatment outline & algorithm

A suggested treatment algorithm is proposed. **Please see** Fig. 2 **[Management Algorithm—Portrait View]**

BBD (Bladder Bowel Dysfunction) and constipation

Bladder and Bowel Dysfunction (BBD)

BBD denotes the presence of concomitant, parallel, bladder and bowel disturbances. BBD has thus replaced the term Dysfunctional Elimination Syndrome (DES), and is now referred to as the umbrella term encompassing both components of Lower Urinary Tract (LUT) dysfunction and bowel dysfunction [2].

Constipation

Controversy exists in the pinpoint diagnosis of **Functional Constipation (FC),** however the international accepted practice largely adheres to the Rome III (now updated Rome IV) criteria [54], for a diagnosis of this condition [2]. The association between FC and LUTS, including enuresis, is well established [2,55]. Thus, the screening of both components, are necessary to exclude BBD [2]. The presence of FC has even shown to be more prevalent in cases of 'Pad Alarm failure' in children with enuresis [56].

Constipation is frequently missed by parents and physicians alike, and a specific history and examination is necessary to elicit this condition [56].

Parents and children should be asked about the frequency of defaecation, the presence of large or painful stools, straining, soiling or leakage of faecal content into the underwear, and retentive behaviour (actively withholding defaecation out of fear for pain). Retentive behaviour may also be a result of a sibling birth, bereavement, school issues, or occult sexual abuse which may be missed during a rushed, scanty history-taking session. During the examination specific attention should be paid to the presence of faecal masses in the suprapubic or left lower quadrants of the abdomen, signifying sigmoid impaction [55].

Stool consistency can be assessed using the **Bristol Stool Chart** or a Bowel Dairy for a period of 7 days.

[links below]:

http://www.sthk.nhs.uk/library/documents/stoolchart.pdf

or

http://static1.1.sqspcdn.com/static/f/1451532/22180508/1363249562587/bristol_stool_chart.pdf

or

http://www.evelinalondon.nhs.uk/resources/patient-information/bladder-bowel-diary.pdf

Commencement of treatment towards the FC should be the initial course of action, as treatment for the associated enuresis may not be needed, if FC is present and adequately dealt with [55].

Recommended treatment options for FC within a South African setting, includes:

Treatment consists of disimpaction with oral and/or rectal laxatives.

Oral polyethylene glycol is currently the preferred treatment, at a suggested dose of 1,5 g/kg/day for disimpaction and 0.8 g/kg/day for maintenance.

Behavioural modification and fluid maintenance with treatment, should aim to keep stools soft [55]. The management of FC in enuresis, is thus listed on the top bar within our proposed Algorithm, (see Treatment **Algorithm** Fig. 2), as the management of FC may result in resolution or better symptom control and management of enuresis in children with co-existing FC.

In the severe, refractory cases of FC, referral to a paediatric gastroenterologist, may be necessary, with plans towards a more thorough evaluation process, which may include: defecography, colon transit measurement and anorectal/colonmanometry [55].

The bladder diary

A bladder diary is also called a frequency: volume chart. In its most basic form it is used to track the number of voids as well as the volume of urine voided. This information is ideally collected over a period of two days, which do not need to be consecutive. A 3 day diary is recommended, however, patient compliance is improved with a 2-day diary compared to a 3-day diary [2,57,58].

Polyuria and constipation may need an extended duration (7 day) Bladder Diary days if suspected, as these issues may only arise on days 4–7 of the assessment period. The night-time voided volume is calculated by adding the first morning voided volume to the increase in the night nappy weight.

The aim of the bladder diary is to objectively record and document bladder function. A complete bladder diary consists of a 7-night recording of incontinence episodes with nocturnal urine volume measurements, accompanied by a 48 h daytime frequency/volume chart (not necessarily two consecutive days). The frequency volume chart is used to assess for the absence/presence of Lower Urinary Tract dysfunction [2,57,58].

Clues to the '3 Systems model' (pathophysiological sub-type) can be explored during the assessment of the bladder diary (see Treatment **Algorithm** Fig. 2).

As a guide, the following Bladder Diaries are suggested (links to the PDF Document):

http://www.monashchildrenshospital.org/wp-content/uploads/2016/10/15050_Bladder_diary_form.pdf

or

https://www.aci.health.nsw.gov.au/__data/assets/pdf_file/0004/155911/enable_bladder_diary.pdf

or

http://www.evelinalondon.nhs.uk/resources/patient-information/bladder-bowel-diary.pdf.

Enuresis and Attention Deficit Hyperactivity Disorder (ADHD)

ADHD does not cause enuresis and enuresis is not listed as a symptom of ADHD. However, several studies indicate an association between these two diagnoses, with a higher incidence rate of enuresis in children with ADHD and an increased prevalence of ADHD in children with enuresis [59,60].

Enuresis and ADHD are both complex problems resulting in a lot of anguish for the child and the parents/caregivers. Both conditions need to be approached with care and compassion. Parents/caregivers should seek assistance and persist with treatment of both conditions for optimal results.

Enuresis and Adeno-Tonsillar Hypertrophy (ATH)

The concept of upper airway obstruction leading to sleep disordered breathing has been well documented in the literature, and ATH has been listed as one of the commonest underlying causes of sleep disordered breathing, in this age group [61]. Various studies have documented an increased prevalence of enuresis in children with ATH [62–64].

Pathophysiology of this association

The pathophysiology of this association may be explained by a few postulated theories, which include; a sup-optimal arousal response, due to sleep fragmentation resulting from disordered breathing during sleep. The presence of an obstructive airway compensates with an increased respiratory effort, which may cause elevated intra-abdominal pressure which may be transmitted to the bladder. Lastly, sleep disordered breathing, in general, may also result in an elevated Atrial Natriuretic Peptide (ANP) and a decreased ADH [65,66]. These above factors may explain why the association of ATH and enuresis, is a more commonly reported entity.

Assessment and management impact

With regard to the assessment and management of the child with ATH, early well designed studies may have proven that the benefit of adenotonsillectomy in children with enuresis, was not significant to result in an improvement of enuresis symptoms [67].

However, the benefit of adeno-tonsillectomy is now more supported with later studies showing vast ranges of improvement in enuresis control post-adenotonsillectomy [62,64,68–73].

Thus, the general examination should include the assessment of the tonsillar crypts for ATH, with referral to our otorhinolaryngology colleagues where necessary.

Additional investigations

Prior to additional investigations, clinicians should consider the reasons for poor treatment response, which includes:

Incorrect alarm use, sleep apnea, occult constipation, social, psychological and emotional factors.

The majority of children do not need further investigations, however amongst the refractory category, and poor responders, triggers for further investigations are decided on an individual case bases [74].

Investigations to consider in this category include:

- bladder ultrasound [Including capacity, bladder wall thickness and post-void residual volume],
- renal ultrasound,
- urine flow rate,
- filling and emptying cystometrogram (Urodynamics Study).
- anorectal manometry.

Definitions of treatment outcome [2]

In the clinical setting, the child and family/care givers should be allowed to define their appropriate benchmarks for treatment success.

In the Academic setting and to maintain a better specialist referral/research platform, a uniform standard of definitions have been proposed:

Initial success:

No-response: <50% reduction.

Partial response: 50–99% reduction.

Complete response: 100% reduction.

Continued success:

No relapse within 6 months after interruption of treatment.

Relapse:

More than one symptom recurrence, per month.

Complete success:

No relapse in two years after interruption of treatment

Conclusion

With an overall incidence above 14%, Enuresis has a major impact on the children of South Africa [8]. An independent, unbiased, national evaluation and treatment guideline, expanding on the previous summarised guideline [1], is proposed.

Recommended/useful links

http://i-c-c-s.org/

http://bedwetting.elsevierresource.com/

http://www.stopbedwetting.org/hcp/resources

http://www.espu.org/

http://www.bapu.org.uk/

http://www.eric.org.uk/

http://www.bedwetting.ie

http://www.continence.org.au/pages/bedwetting.html

http://www.rch.org.au

http://www.gosh.nhs.uk

http://www.uptodate.com/contents/nocturnal-enuresis-in-children-management

https://www.bladderandbowelfoundation.org/bladder/bladder-conditions-and-symptoms/nocturnal-enuresis/

https://www.healthychildren.org/English/health-issues/conditions/genitourinary-tract/Pages/Nocturnal-Enuresis-in-Teens.aspx

http://svenskaenures.se/?language=en

http://www.spuonline.org/

http://www.drydawn.com

https://www.worldbedwettingday.com/

Disclaimer

This publication is intended for educational and medical related purposes only. The recommendations are based on currently available scientific evidence together with the consensus opinion of the listed authors. Adherence to these recommendations is voluntary and does not account for individual variation among patients; the recommendations are not intended to supplant physician judgement with respect to particular patients or special clinical situations. In addition, these recommendations do not indicate an exclusive diagnostic workup or course of treatment or serve as the standard of medical care.

Ethical committee approval

Not applicable.

Conflict of interests

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Nestle Nutrition Institute for lectures [unrelated to this guideline]

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Aniruddh Deshpande

Departmental Educational grant by Ferring Australia to update enuresis resource kit [unrelated to this current guideline]

Agency for clinical innovation Collaborative Group of Urinary Incontinence in Children, Australia

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Authors' contributions

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.afju.2017.07.002.

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